

## **AMENDMENT TO THE CLAIMS**

After entry into the U.S. national stage, and assurance of a U.S. filing date, the present document amends the claims from the PCT application by amending claim 75 and adding claims 79-82. According to 37 C.F.R. § 1.121(c), after entry of the present amendment, the status of the claims in the case is as follows:

1. (Original) A method for performing optical imaging or treatment of at least a first tissue in an animal, comprising providing into the blood associated with said at least a first tissue a biologically effective amount of a low-scattering, oxygen-carrying blood substitute, and applying an optical imaging or treatment step to said at least a first tissue.
2. (Original) The method of claim 1, wherein said low-scattering, oxygen-carrying blood substitute is a substantially non-particulate hemoglobin solution.
3. (Original) The method of claim 2, wherein said hemoglobin solution is a substantially non-particulate, homogeneous, acellular hemoglobin solution.
4. (Original) The method of claim 2, wherein said hemoglobin solution comprises bovine, porcine, ovine or primate hemoglobin.
5. (Original) The method of claim 2, wherein said hemoglobin solution comprises human hemoglobin.

6. (Original) The method of claim 2, wherein said hemoglobin solution comprises recombinantly produced hemoglobin.
7. (Original) The method of claim 2, wherein said hemoglobin solution comprises crosslinked hemoglobin.
8. (Original) The method of claim 2, wherein said hemoglobin solution comprises polymerized hemoglobin.
9. (Original) The method of claim 2, wherein said hemoglobin solution comprises glutaraldehyde crosslinked, polymerized hemoglobin.
10. (Original) The method of claim 2, wherein said hemoglobin solution comprises surface modified hemoglobin.
11. (Original) The method of claim 2, wherein said hemoglobin solution has a hemoglobin concentration of at least about 70% of the hemoglobin concentration of whole blood.
12. (Original) The method of claim 1, wherein provision of said low-scattering, oxygen-carrying blood substitute reduces the hematocrit of the blood associated with said at least a first tissue at least to about 10%.

13. (Original) The method of claim 12, wherein provision of said low-scattering, oxygen-carrying blood substitute reduces the hematocrit of the blood associated with said at least a first tissue at least to about 5%.

14. (Original) The method of claim 13, wherein provision of said low-scattering, oxygen-carrying blood substitute reduces the hematocrit of the blood associated with said at least a first tissue at least to about 4%.

15. (Original) The method of claim 14, wherein provision of said low-scattering, oxygen-carrying blood substitute reduces the hematocrit of the blood associated with said at least a first tissue at least to about 3%.

16. (Original) The method of claim 15, wherein provision of said low-scattering, oxygen-carrying blood substitute reduces the hematocrit of the blood associated with said at least a first tissue at least to about 2%.

17. (Original) The method of claim 16, wherein provision of said low-scattering, oxygen-carrying blood substitute reduces the hematocrit of the blood associated with said at least a first tissue at least to about 1%.

18. (Original) The method of claim 1, wherein provision of said low-scattering, oxygen-carrying blood substitute reduces the hematocrit of the blood associated with said at least a first tissue to between 0 and about 10%.

19. (Original) The method of claim 18, wherein provision of said low-scattering, oxygen-carrying blood substitute reduces the hematocrit of the blood associated with said at least a first tissue to between 1 and about 5%.

20. (Original) The method of claim 1, wherein provision of said low-scattering, oxygen-carrying blood substitute reduces the hematocrit of the blood associated with said at least a first tissue to an amount effective to result in a half maximal or lower scattering coefficient as shown in FIG. 1B.

21. (Original) The method of claim 1, wherein provision of said low-scattering, oxygen-carrying blood substitute reduces the hematocrit of the blood associated with said at least a first tissue to an amount effective to result in a scattering coefficient of about half the scattering coefficient for whole blood or less.

22. (Original) The method of claim 1, wherein said low-scattering, oxygen-carrying blood substitute is a solution comprising at least a first oxygen carrier, and wherein the largest species in said solution has a size of about 6 nanometers.

23. (Original) The method of claim 1, wherein provision of said low-scattering, oxygen-carrying blood substitute reduces the scattering coefficient of the blood associated with said at least a first tissue to about one half of the scattering coefficient of whole blood or less at a sample wavelength of between about 600 nm and about 1500 nm.

24. (Original) The method of claim 23, wherein provision of said low-scattering, oxygen-carrying blood substitute reduces the scattering coefficient of the blood associated with said at least a first tissue to about one tenth of the scattering coefficient of whole blood or less at a sample wavelength of between about 600 nm and about 1500 nm.

25. (Original) The method of claim 23, wherein provision of said low-scattering, oxygen-carrying blood substitute reduces the scattering coefficient of the blood associated with said at least a first tissue to about one half of the scattering coefficient of whole blood or less at a sample wavelength of about 600 nm.

26. (Original) The method of claim 25, wherein provision of said low-scattering, oxygen-carrying blood substitute reduces the scattering coefficient of the blood associated with said at least a first tissue to about one tenth of the scattering coefficient of whole blood or less at a sample wavelength of about 600 nm.

27. (Original) The method of claim 23, wherein provision of said low-scattering, oxygen-carrying blood substitute decreases the scattering coefficient of the blood associated with said at least a first tissue to a scattering coefficient of about  $0.4 \text{ mm}^{-1}$  or less at about 1310 nm.

28. (Original) The method of claim 27, wherein provision of said low-scattering, oxygen-carrying blood substitute decreases the scattering coefficient of the blood associated with said at least a first tissue to a scattering coefficient of about  $0.3 \text{ mm}^{-1}$  or less at about 1310 nm.

29. (Original) The method of claim 28, wherein provision of said low-scattering, oxygen-carrying blood substitute decreases the scattering coefficient of the blood associated with said at least a first tissue to a scattering coefficient of about  $0.2 \text{ mm}^{-1}$  at about 1310 nm.
30. (Original) The method of claim 1, wherein said low-scattering, oxygen-carrying blood substitute is a solution comprising at least a first oxygen carrier, and wherein the refractive index of said oxygen carrier is substantially equal to other molecular species in solution.
31. (Original) The method of claim 1, wherein said low-scattering, oxygen-carrying blood substitute has at least about 70% of the oxygen carrying capacity of whole blood.
32. (Original) The method of claim 1, wherein said optical imaging or treatment step applies light of a wavelength of between about 600 nm and about 1500 nm.
33. (Original) The method of claim 1, wherein an optical imaging step is performed on said at least a first tissue.
34. (Original) The method of claim 33, wherein said optical imaging step generates an image by light transmitting through said at least a first tissue.
35. (Original) The method of claim 33, wherein said optical imaging step generates an image by light reflected by said at least a first tissue.

36. (Original) The method of claim 33, wherein said optical imaging step is a spectroscopic imaging step.

37. (Original) The method of claim 36, wherein said spectroscopic imaging step is reflectance spectroscopy.

38. (Original) The method of claim 36, wherein said spectroscopic imaging step is fluorescence spectroscopy.

39. (Original) The method of claim 36, wherein said spectroscopic imaging step is resonance spectroscopy.

40. (Original) The method of claim 39, wherein said spectroscopic imaging step is Raman spectroscopy.

41. (Original) The method of claim 33, wherein said optical imaging step is a photoacoustic imaging step.

42. (Original) The method of claim 33, wherein said optical imaging step is a non-linear harmonic imaging step.

43. (Original) The method of claim 33, wherein said optical imaging step is a photothermal imaging step.
44. (Original) The method of claim 33, wherein said optical imaging step is an optical coherence tomography (OCT) imaging step.
45. (Original) The method of claim 33, wherein said optical imaging step provides a spatial image of said at least a first tissue.
46. (Original) The method of claim 33, wherein said optical imaging step provides a temporal image of said at least a first tissue.
47. (Original) The method of claim 33, further comprising performing at least a first treatment based upon the image provided in said optical imaging step.
48. (Original) The method of claim 47, wherein said at least a first treatment comprises a surgical treatment step.
49. (Original) The method of claim 47, wherein said at least a first treatment comprises an optical treatment step.
50. (Original) The method of claim 1, wherein an optical treatment step is performed on said at least a first tissue.



51. (Original) The method of claim 50, wherein said optical treatment step is a laser ablation treatment step.

52. (Original) The method of claim 50, wherein said optical treatment step is a laser angioplasty treatment step.

53. (Original) The method of claim 50, wherein said optical treatment step is a laser photothermolysis treatment step.

54. (Original) The method of claim 50, wherein said optical treatment step is a photoacoustic treatment step.

55. (Original) The method of claim 1, wherein said optical imaging or treatment step comprises a light refraction step.

56. (Original) The method of claim 1, wherein optical imaging and treatment steps are each performed on said at least a first tissue.

57. (Original) The method of claim 1, wherein said at least a first tissue is neural tissue.

58. (Original) The method of claim 1, wherein said at least a first tissue is brain tissue.

59. (Original) The method of claim 1, wherein said at least a first tissue is located within a highly perfused organ.

60. (Original) The method of claim 59, wherein said at least a first tissue is located within the kidney, lung, liver, spleen, brain, heart or one of the great vessels.

61. (Original) The method of claim 1, wherein said at least a first tissue is cardiovascular tissue.

62. (Original) The method of claim 1, wherein said at least a first tissue is cardiac tissue.

63. (Original) The method of claim 1, wherein said at least a first tissue is a blood vessel.

64. (Original) The method of claim 63, wherein said optical imaging or treatment step is applied from the lumen of said blood vessel.

65. (Original) The method of claim 63, wherein said blood vessel has or is suspected to have an atherosclerotic plaque or lesion.

66. (Original) The method of claim 1, wherein said at least a first tissue comprises at least two tissue layers, and wherein at least a first of said tissue layers is associated with a substantial blood fraction.

67. (Original) The method of claim 66, wherein said at least a first tissue comprises a plurality of tissue layers, and wherein at least a first of said tissue layers is associated with a substantial blood fraction.

68. (Original) The method of claim 1, wherein said animal has, or is at risk for developing, a cardiac tissue or cardiac valve defect.

69. (Original) The method of claim 1, wherein said animal has suffered, or is at risk for developing, a heart attack.

70. (Original) The method of claim 1, wherein said animal has, or is at risk for developing, an ischemic tissue.

71. (Original) The method of claim 1, wherein said animal has suffered, or is at risk for developing, a stroke.

72. (Original) The method of claim 1, wherein said animal has, or is at risk for developing, a vascularized tumor.

73. (Original) The method of claim 1, wherein said animal is a mouse.

74. (Original) The method of claim 1, wherein said animal is a human subject.

75. (Currently Amended) A method for optical coherence tomography imaging of a tissue in an animal ~~that~~ , which tissue comprises a substantial blood fraction, comprising:

- (a) introducing into said blood fraction of said tissue an amount of an essentially non-particulate hemoglobin solution effective to substantially reduce optical scattering from said blood fraction whilst substantially maintaining oxygenation in said tissue; and
- (b) performing optical coherence tomography imaging of said tissue.

76. (Original) A kit comprising a low-scattering, oxygen-carrying blood substitute and instructions for using said blood substitute in an optical imaging or treatment method.

77. (Original) The kit of claim 76, wherein said instructions are written instructions.

78. (Original) The kit of claim 76, wherein said instructions are computerized instructions.

79. (New) A method for performing optical imaging or treatment of a tissue in an animal, which tissue comprises a substantial blood fraction, comprising:

- (a) introducing into said blood fraction of said tissue an amount of a low-scattering, oxygen-carrying blood substitute effective to substantially reduce optical scattering from said blood fraction whilst substantially maintaining oxygenation in said tissue; and
- (b) applying an optical imaging or treatment step to said tissue.

80. (New) A method for performing optical imaging of at least a first tissue in an animal, comprising providing into the blood associated with said at least a first tissue a biologically effective amount of a low-scattering, oxygen-carrying blood substitute, and applying an optical imaging step to said at least a first tissue.

81. (New) A method of generating an image of at least a first vascularized tissue by *in vivo* diagnostic light imaging, comprising providing into the blood perfusing said vascularized tissue a biologically effective amount of a low-scattering, oxygen-carrying blood substitute, and executing a diagnostic light imaging technique to generate an image of said vascularized tissue.

82. (New) A method for optical coherence tomography imaging of at least a first tissue in an animal, comprising providing into the blood associated with said at least a first tissue a biologically effective amount of a substantially non-particulate hemoglobin solution, and performing optical coherence tomography imaging of said at least a first tissue.